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10/591,558	06/08/2007	Irun R. Cohen	2488.041	3088

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EXAMINER	
NOBLE, MARCIA STEPHENS	
ART UNIT	PAPER NUMBER
1632	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,558	COHEN ET AL.	
	Examiner	Art Unit	
	MARCIA S. NOBLE	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32,49 and 50* is/are pending in the application.

4a) Of the above claim(s) *10-32, 49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-32, 49, and 50 are pending. Claims 1, 7, 8, 10, and 22 are amended, claims 33-48 are canceled, and claims 49 and 50 are newly added by the amendment filed 5/22/2008.

Election/Restrictions

2. Applicant's election with traverse of Group I, claims 1-9, in the reply filed on 5/22/2008 is acknowledged. The traversal is on the ground(s) that newly amended claim 1 now encompasses a eukaryotic expression vector and Kokuho et al, which was used to demonstrate a lack of special technical feature, discloses a non-eukaryotic expression vector. Applicant asserts that Kokuho et al no longer discloses the invention of claim 1 and therefore no longer demonstrates a lack of special technical feature. Applicant asserts that the restriction should be withdrawn in view of the amendment to the claims and because Kokuho et al longer is no longer applicable to the instant invention (p. 6, par 5 to p. 7, last par). This is not found persuasive because, even though the amendment to the claims differentiates the disclosures of Kokuho et al from the instant invention of claim 1, other arts demonstrate that the invention of claim 1 lacks a special technical feature, as will be demonstrated by the rejections that follow.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-32, 49 and 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/22/2008.

Claims 49 and 50 are newly added claims drawn to the methods of Group II and therefore would be considered with Group II. Claims 49 and 50 are therefore withdrawn with the claims of Group II because the claims of Group I are the claims under consideration. Claims 1-9 are under consideration.

Information Disclosure Statement

3. The information disclosure statement filed 8/31/2006 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the reference present in the IDS filed 8/31/2006 has already been considered in the IDS filed 3/26/2008. Therefore the IDS filed 8/31/2006 is a duplicate of the IDS 3/26/2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a recombinant construct comprising an isolated nucleic acid sequence encoding an antigen selected from CD25, homologs and fragments thereof; the nucleic acid sequence being operably linked to one or more transcription control sequences, wherein said recombinant

construct is an eukaryotic expression vector; and a pharmaceutically acceptable carrier, adjuvant, excipient, or diluent, does not reasonably provide enablement for a DNA vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is “undue”.

The instant claims are drawn to a DNA vaccine. According to Dictionary.com (www.dictionary.reference.com/browse/vaccine), a “vaccine" is defined as "any preparation used as a preventive inoculation to confer immunity against a specific disease" (see definition # 1).

The specification discloses that the purpose of the instant invention is to provide effective DNA vaccinations for T cell mediated autoimmune disease (p. 11, lines 4-5). The specification discloses that T cell lines generated by vaccination with peptide

derived from CD25 were suggested to be involved in protection from experimentally-induced autoimmune encephalomyelitis (p. 2, lines 9-12). The specification teaches that CD25 DNA administration induced a low but significant IgG response to two CD25 peptides present in rats with adjuvant-induced arthritis (p. 26, Example 3, lines 24-26). The specification teaches that the administration of CD25 DNA induced a T cell proliferative response in drained lymph node cells in rats with adjuvant-induced arthritis (p. 27, lines 9-12).

However, the specification fails to demonstrate that the administration of the CD25 DNA vector results in the prevention or treatment of symptoms associated with an autoimmune disease. The specification fails to provide evidence to teach that the administration of the CD25 vector convey immunity against an autoimmune disease. Therefore, the specification fails to provide specific guidance to teach that the CD25 expression vector of the instant invention serves as a vaccine because CD25 does not provide immunity to a disease.

Furthermore, the art suggests that the achieving a protective immune response from a DNA vaccine is unpredictable in the art . Van Drunden Little-Van den Hurk et al (Immuno Rev 199:113-125, 2004) teaches that no DNA vaccine have been approved for medicinal use because there inefficiency or lack of producing a protective immune response (p. 114, par bridging col 1 and 2).

In summary, the instant invention is not enabled for the full breadth of the claim to a DNA vaccine because the specification fails to provide specific guidance to demonstration that CD25 expression vector of the instant invention functions as a

vaccine (i.e.- confers immunity to a disease). Furthermore, the art teaches that the induction of a protective immune response from a DNA vaccine is unpredictable. Therefore, because the specification fails to provide specific guidance to predictably produce a CD25 DNA vaccine capable of conferring immunity to a disease with a reasonable expectation of success and without undue experimentation, the instant claims are only enabled for composition comprising a recombinant construct comprising an isolated nucleic acid sequence encoding an antigen selected from CD25, homologs and fragments thereof; the nucleic acid sequence being operably linked to one or more transcription control sequences, wherein said recombinant construct is an eukaryotic expression vector; and a pharmaceutically acceptable carrier, adjuvant, excipient, or diluent.

Claim Rejections - 35 USC § 102

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3-6, and 9 rejected under 35 U.S.C. 102(b) as being anticipated by Kokuho et al (Immunology and Cell Biology 75(5):515-518, 1997).

The structural components of the instantly claimed composition comprise a eukaryotic expression vector comprising a nucleic acid sequence encoding a CD25 operably linked to a transcriptional control sequence. The preamble of the claims recites that the composition is a DNA vaccine. However, if the structural components of the claimed invention are disclosed in the prior art, the limitations of the claims have

been met regardless of whether the claimed vector is used as a DNA vaccine or another use.

Kokuho et al discloses a COS expression vector, pcDNA3.1/Zeo(+), comprising the coding sequence of porcine IL-2R alpha (p. 515, col 2, last two lines to p. 516, col 1, line 1). The specification discloses that IL2-R alpha is CD25 (see page 4, line 12 of the specification). Kokuho et al discloses that this expression vector had been transfected into COS-7 cells, which are eukaryotic cells (p. 516, col 1, lines 2-3). Therefore, this COS expression vector is a eukaryotic expression vector as claimed. Kokuho et al discloses that the COS-7 cells successfully express the IL-2R alpha protein encoded by the construct (abstract and p. 517, col 1, 1st full par, lines 1-7). Therefore, inherently the COS expression vector of Kokuho et al comprises operable linkage to a transcriptional control sequence, as claimed. These disclosures of Kokuho et al encompass the limitations of claims 1, 5, and 9. Claims 3 and 4 specific the CD25 sequence comprising the nucleic acid sequence of SEQ NO:1 and encoding the amino acid sequence of SEQ ID NO:2. However, claim 1 specifies the nucleic acid encoding CD25 as the entire sequence, homologs, and fragments thereof. A “fragment” only requires two or three nucleotides in common with a disclosed sequence to meet the limitations of a “fragment”. Therefore, Kokuho et al discloses a fragment of SEQ ID NO: 1 that encodes a fragment of SEQ ID NO:2 as claimed. Claim 6 specifies that the composition comprises the structural component of a liposome, micelles, emulsions, or cells. The disclosure of the transfected COS-7 cells comprising COS expression vector encoding the IL-2R alpha encompasses the limitations of claim 6.

6. Claims 1- 6, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al (Zhongguo yi xue ke xue yuan xue bao. Acta Academiae Medicinae Sinicae 17(5);326-332, abstract; 1995).

The structural components of the instantly claimed composition comprise a eukaryotic expression vector comprising a nucleic acid sequence encoding a human CD25 operably linked to a transcriptional control sequence. The preamble of the claims recites that the composition is a DNA vaccine. However, if the structural components of the claimed invention are disclosed in the prior art, the limitations of the claims have been met regardless of whether the claimed vector is used as a DNA vaccine or another use.

Cheng et al discloses a pRc/CMV eukaryotic expression vector encoding a fragment of the human IL-2 receptor alpha (abstract). The specification discloses that IL2-R alpha is CD25 (see page 4, line 12 of the specification). This disclosure of Cheng et al encompasses the limitations of claims 1, 2, 5, and 7. Claims 3 and 4 specific the CD25 sequence comprising the nucleic acid sequence of SEQ NO:1 and encoding the amino acid sequence of SEQ ID NO:2. However, claim 1 specifies the nucleic acid encoding CD25 as the entire sequence, homologs, and fragments thereof. A “fragment” only requires two or three nucleotides in common with a disclosed sequence to meet the limitations of a “fragment”. Therefore, Chen et al discloses a fragment of SEQ ID NO: 1 that encodes a fragment of SEQ ID NO:2 as claimed. Claim 6 specifies that the composition comprises the structural component of a liposome, micelles, emulsions, or

cells. Cheng et al discloses that the in expression vector was transfected and expressed in CHO cells. Therefore, Cheng et al discloses the limitations of claim 6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al (Zhongguo yi xue ke xue yuan xue bao. Acta Academiae Medicinae Sinicae 17(5);326-332, abstract; 1995), in further view of NM_00417 (NCBI Entrez Nucleotide. Hafler et al; http:www.ncbi.nlm.nih.gov/entrez/viewer/fcgi?db=nuccore&id=4557666, see printout pages 1-5; of record), NP_000408 (NCBI Entrez Protein. Hafler et al. http:www.ncbi.nlm.nih.gov/entrez/viewer/fcgi?db=Protein&id=4557667, see printout pages 1-4; of record), and Karin et al (US Pat No. 6,316,420 issue date: 12/3/2001; of record).

Cheng et al teaches a pRc/CMV eukaryotic expression vector encoding a fragment of the human IL-2 receptor alpha (abstract). The specification discloses that IL2-R alpha is CD25 (see page 4, line 12 of the specification). This teaching of Cheng et al encompasses the limitations of claims 1, 2, 5, and 7. Claim 6 specifies that the composition comprises the structural component of a liposome, micelles, emulsions, or cells. Cheng et al teaches that the in expression vector was transfected and expressed

in CHO cells (abstract). Therefore, Cheng et al teaches the limitations of claim 6. Cheng et al also teaches that the establishment of rhsIL-2R alpha expressing cell lines is of importance in the detection and purification of IL-2 based on the ability of affinity binding between IL-2 and its recombinant receptor (abstract). Therefore, Cheng et al teach a motivation for producing expression vectors encoding CD25.

Cheng et al does not specifically teach that the nucleic acid encoding CD25 is the sequence of SEQ ID NO:1, as claimed in claim 3. Cheng et al also does not specifically teach that the amino acid encoded by the vector comprises the sequence of SEQ ID NO:2, as claimed in claims 4 and 8. However, the specification teaches that SEQ ID NO:1 corresponds to gi:4557666 and SEQ ID NO:2 corresponds to gi:4557667. NM_000417 from NCBI entrez Nucleotide teaches a nucleic acid sequence corresponding to gi: 4557666 and teaches that this sequence was present in the prior art as early as 1990 (see p. 2 of the printout). NP_000408 from NCBI entrez Protein teaches an amino acid sequence corresponding to gi: 4557667, and teaches that this sequence was present in the prior art as early as 1986 (see p. 2 of the printout). Therefore, at the time of the invention, NM_000417 and NP_000408 teach that SEQ ID NO:1 and SEQ ID NO:2 was established in the prior art.

Cheng et al does not specifically teach all of the carriers, such as liposomes, micelles, and emulsions, as claimed in claim 6. However, Karin et al teach that liposomes, micelles, and emulsions, can be employed as carriers to deliver DNA vaccine expression vectors (col 4, lines 18-20). Therefore, at the time of the invention,

all the claimed carriers and their use for delivering expression vectors were established in the prior art, as taught by Karin et al.

Cheng et al also does not teach the transcriptional control sequences, RSV control sequences, retroviral LTR sequences, SV-40 control sequences, and beta-actin control sequences, as specified in claim 8. However, Karin et al teaches expression vectors used to deliver DNA vaccines (col 3, lines 62-67). Karin et al teaches suitable promoters which may be employed in expression vectors include retroviral LTR, the SV40 promoter, CMV promoter, and beta-actin promoter (col 4, lines 43-48). Therefore, at the time of the invention, all of the claim transcriptional control sequences and their use in expression vectors were established in the prior art, as taught by Karin et al.

Cheng et al also does not teach all eukaryotic expression vectors, pcDNA3, pZeoSV2, pSecTag2, pDisplay, pEF/myc/cyto, pCMV/myc/cyto, pCR3.1, pCI, pBK-RSV, pBK-CMV, and pTRES, as specified in claim 9. However, Karin et al teaches that the recombinant construct for the production of a DNA vaccine can be selected from the group consisting of pcDNA3, pcDNA3.1(+/-), pZeoSV2(+/-), pSecTag2, pDisplay, pEF/myc/cyto, pCMV/myc/cyto, pCR3.1, pCI, pBK-RSV, pBK-CMV, and pTRES (col 4, lines 53-58). Therefore, at the time of the invention, the eukaryotic expression vectors were established in the prior art, as taught by Karin et al.

Karin et al also teaches pharmaceutically acceptable carriers (col 4, lines 1-7).

Therefore, it would have been obvious to an artisan of ordinary skill at the time the invention was made to choose from a finite number of predictable CD25 sequences, as taught by NM_000417 and NP_000408, and a finite number of predicable carriers,

transcriptional control sequences, and eukaryotic expression vectors as taught by Karin et al, with a reasonable expectation of successfully producing an eukaryotic expression vector variant of Cheng et al comprising a nucleic acid encoding a CD25 operably linked to a transcriptional control sequence and a pharmaceutically acceptable carrier. Therefore, because the prior art of Cheng et al, NM_000417 and NP_000408, and Karin et al demonstrate that the components of the instantly claimed expression vector were established in art and predictably can be combined to produce the instantly claimed expression vector, the prior art of Cheng et al, NM_000417 and NP_000408, and Karin et al render the instant claims obvious over the prior art.

It is noted that Karin et al teaches DNA vaccines. However, Karin et al was used for its general teaches of the various expression vectors, carriers, and pharmaceutically acceptable carrier established in the art.

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcia S. Noble

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